

**RICHARD S. GEARY, Ph. D.**

**EDUCATION:**

Ph.D., Pharmaceutics, University of Texas at Austin, 1988

B.S., Biology, Texas A&M University, 1980

**PROFESSIONAL POSITIONS AND EXPERIENCE:**

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|--------------|---|
| 2008-Present | Senior Vice President of Development, Isis Pharmaceuticals<br><i>Job Description:</i> Responsible for preclinical and clinical development of antisense drugs.  |
| 2003-2008    | Vice President of Pharmacokinetics and Metabolism, Isis Pharmaceuticals, Department of Toxicology and Pharmacokinetics<br><i>Job Description:</i> Provide direction and support for preclinical and clinical development of oligonucleotide therapeutics. |
| 2001-2003    | Executive Director of Pharmacokinetics, Isis Pharmaceuticals, Department of Toxicology and Pharmacokinetics   |
| 1998-2001    | Director of Pharmacokinetics, Isis Pharmaceuticals, Department of Toxicology and Pharmacokinetics   |
| 1997-1998    | Associate Director of Pharmacokinetics, Isis Pharmaceuticals, Department of Toxicology and Pharmacokinetics   |
| 1995-1997    | Assistant Director of Pharmacokinetics, Isis Pharmaceuticals, Department of Toxicology and Pharmacokinetics   |
| 1993-1995    | Manager, Southwest Research Institute, Applied Biopharmaceutics and Physical Chemistry, Department of Applied Chemistry and Chemical Engineering  |
| 1992-1993    | Group Leader, Southwest Research Institute, Pharmaceutics and Pharmacology Section, Department of Applied Chemistry and Chemical Engineering  |
| 1990-1992    | Senior Research Scientist, Southwest Research Institute, Pharmaceutics and Pharmacology Section, Department of Applied Chemistry and Chemical Engineering   |

1987-1990      Research Scientist, Southwest Research Institute, Pharmaceuticals and  
Pharmacology Section, Department of Applied Chemistry and Chemical  
Engineering

**CONTINUING EDUCATION COURSES:**

Incorporation of Pharmacokinetic and Pharmacodynamic Data into Risk Assessment, Nashville,  
TN, SOT, 2002

Prediction of Human Toxicity and Metabolic Fate of Drugs Using In Vitro Systems, San  
Francisco, CA, SOT, 2001

Advances in Non-Invasive Micrometer and Nanometer Scale Cellular/Tissue Vital Imaging,  
Philadelphia, PA, SOT, 2000

Toxicokinetics and Physiologically-Based Toxicokinetics in Toxicology and Risk Assessment,  
Philadelphia, PA, SOT, 2000

Advanced Topics in Toxicokinetics, Anaheim, CA, SOT, 1996

New Approaches for Studying Cytochrome P450-Dependant Toxicant Metabolism, Anaheim,  
CA, SOT, 1996

Application of Pharmacokinetics to Toxicological Testing, Dallas, TX, SOT, 1994

Implementing PBPK Models, Dallas, TX, SOT, 1991

Introduction to Physiologically-based Pharmacokinetic Modeling, Dallas, TX, SOT, 1991

**TRAINING COURSES:**

Understanding GLP's (Video), 1998

Short Course in Population Pharmacokinetics Data Analysis using the NONMEM System, April  
20-22, 1998

Performance Management and Appraisal Training Program – The Coach Approach, 1997

Population Pharmacokinetics and P-Pharm Workshop, April 1-3, 1996

GLP Training – SwRI 1992-1995

Total Quality Management – SwRI 1993

**BOOKS AND CHAPTERS:**

Bennett, C. F., Swayze, E., Geary, R., Henry, S., Tillman, L., Hardee, G. (2008) Antisense Oligonucleotide-based Therapeutics. Gene and Cell Therapy: Mechanisms and Strategies. 497-522

Yu, R. Z., Geary, R. S., and Levin, A. A. (2007). Pharmacokinetics and Pharmacodynamics of Antisense Oligonucleotides. In Encyclopedia of Molecular Cell biology and Molecular Medicine (R. A. Meyers, ed. Wiley-VCH, Weinheim, Germany.

Geary, R. S., Yu, R. Z., Siwkowski, A., and Levin, A. A. (2007). Pharmacokinetic/Pharmacodynamic Properties of Phosphorothioate 2' - O-(2-Methoxyethyl)-Modified Antisense Oligonucleotides in Animals and Man. In Antisense Drug Technology, Principles, strategies and applications. S. T. Crooke, ed., Vol. 2, pp. 305-326. Taylor & Francis Group, Boca Raton, FL.

Hardee, G. E., Tillman, L. G., and Geary, R. S. (2007). Routes and Formulations for Delivery of Antisense Oligonucleotides. In Antisense Drug Technology, Principles, strategies and applications. S. T. Crooke, ed., Vol. 2, pp. 217-236. Taylor & Francis Group, Boca Raton, FL.

Levin, A. A., Yu, R. Z., and Geary, R. S. (2007). Basic Principles of the Pharmacokinetics of Antisense Oligonucleotide Drugs. In Antisense Drug Technology, Principles, strategies and applications. S. T. Crooke, ed., Vol. 2, pp. 183-215. Taylor & Francis Group, Boca Raton, FL.

Yu, R., Geary, R.S., Watanabe, T., Levin, A.A., Schoenfeld, L.S., Pharmacokinetic properties in humans. Antisense Drug Technology: Principles, Strategies, and Applications. (2001) Marcel Dekker, Inc. 183-200.

Geary, R.S., Yu, R., Leeds, J.M., Watanabe, T., Henry, S.P., Levin, A.A., Templin, M.V. Pharmacokinetic properties in animals. Antisense Drug Technology. Principles, Strategies, and Applications. (2001) Marcel Dekker, Inc. 119-154.

Bennett, F.C., Büttler, M., Cook, D.P., Geary, R.S., Levin, A.A., Mehta, R., Teng, C.L., Deshmukh, H., Tillman, L., Hardee, G. (2000) Antisense oligonucleotide-based therapeutics. Gene Therapy. Marcel Dekker, Inc. 305-332.

Levin, A.A., Geary, R.S., Leeds, J.M., Monteith, D.K., Yu, R., Templin, M.V. and Henry, S.P., (1998). The pharmacokinetics and toxicity of phosphorothioate oligonucleotides. Biotechnology and Safety Assessment, Taylor & Francis. 1: 151-175.

Levin, A.A., Monteith, D.K., Leeds, J.M., Nicklin, P.L., Geary, R.S., Butler, M., Templin, M.V. and Henry, S.P., (1998). Toxicity of oligodeoxynucleotide therapeutic agents. *Antisense Research and Application*. Croke, S.T. Heidelberg, Springer. 131: 169-215.

Leeds, J.M. and Geary, R.S., (1998). Pharmacokinetic properties of phosphorothioate oligonucleotides in humans. *Antisense Research and Application*. Croke, S.T. Heidelberg, Springer. 131: 217-232.

Geary, R.S., (1993). Drug delivery systems and recombinant proteins. *Biotechnology and Safety Assessment*, Raven, New York, NY.

### **PROFESSIONAL PUBLICATIONS:**

Geary RS. (2009) Antisense Oligonucleotide Pharmacokinetics and Metabolism. Expert Opinion, Drug Metabolism & Toxicology. 2009 Apr;5(4):381-91.

Geary RS, Wanciewicz E, Matson J, Pearce M, Siwkowski A, Swayze E, Bennett F. (2009) Effect of Dose and Plasma Concentration on Liver Uptake and Pharmacologic Activity of a 2'-Methoxyethyl Modified Chimeric Antisense Oligonucleotide Targeting PTEN. *Biochemical Pharmacology*. 2009 Apr 21 published online. Currently in press.

Yu R.Z., Lemonidis K.M., Graham M.J., Matson J.E., Croke R.M., Tribble D.L., Wedel M.K., Levin A.A., Geary R.S. (2009) Cross-species comparison of In Vivo PK/PD relationships for second generation antisense oligonucleotides targeting apolipoprotein B-100. *Biochemical Pharmacology*. 2009 March, 77 (5) 910-919.

Yu R.Z., Geary R.S., Flaim J., Riley G., Tribble D., van Vliet A., Wedel M. (2009) Lack of Pharmacokinetic Interaction of Mipomersen Sodium (ISIS 301012), a 2'-O-Methoxyethyl Modified Antisense Oligonucleotide Targeting Apolipoprotein B-100 Messenger RNA, with Simvastatin and Ezetimibe. *Clinical Pharmacokinetics*. 2009; 48 (1): 39-50.

Crosby J.R., Guha M., Tung D., Miller D.A., Bender B., Condon T.P., York-Defalco C., Geary R.S., Monia B.P., Karras J.G., Gregory S.A. (2007). Inhaled CD86 Antisense Oligonucleotide Suppresses Pulmonary Inflammation and Airway Hyper-responsiveness in Allergic Mice. *J Pharm Sci*. 2008 Jan; 97 (1): 225-36.

Tillman L.G., Geary R.S., and Hardee G.E. (2007). Oral Delivery of Antisense Oligonucleotides In Man. *J Pharm Sci*. 2008 Jan; 97 (1): 225-36.

Yu R.Z., Kim T.W., Hong A., Watanabe T.A., Gaus H.J., and Geary R.S. (2007). Cross-Species Pharmacokinetic Comparison from Mouse to Man of a Second Generation Antisense Oligonucleotide ISIS 301012, Targeting Human ApoB-100. *Drug Metab. Dispos*. 35, 460-468.

Karras J.G., Crosby J.R., Guha M., Tung D., Miller D.A., Gaarde W.A., Geary R.S., Monia B.P., and Gregory S.A. (2007). Anti-inflammatory activity of inhaled IL-4 receptor-alpha antisense oligonucleotide in mice. *Am J Respir Cell Mol Biol* 36, 276-85.

Geary R.S., Bradley J.D., Watanabe T., Kwon Y., Wedel M., van Lier J.J., vanVliet A.A. (2006). Lack of Pharmacokinetic Interaction for ISIS 113715, a 2'-O-Methoxyethyl Modified Antisense Oligonucleotide Targeting Protein Tyrosine Phosphatase 1B Messenger RNA, with Oral Antidiabetic Compounds Metformin, Glipizide or Rosiglitazone. *Clinical Pharmacokinetics*: Volume 45(8)2006pp 789-801.

Miner P.B., Jr., Geary R.S., Matson J., Chuang E., Xia S., Baker B.F., and Wedel M.K. (2006). Bioavailability and therapeutic activity of alicaforsen (ISIS 2302) administered as a rectal retention enema to subjects with active ulcerative colitis. *Aliment Pharmacol Ther* 23, 1427-1434.

Watanabe, T.A., Geary, R.S., and Levin, A.A. (2006). Plasma Protein Binding of an Antisense Oligonucleotide Targeting Human ICAM-1 (ISIS 2302). *Oligonucleotides* 16, 169-180.

Soucy, N.V., Riley J.P., Templin, M.V., Geary, R.S., de Peyster, A., and Levin, A.A. (2006). Maternal and fetal distribution of a phosphorothioate oligonucleotide in rats after intravenous infusion. *Birth Defects Res B Dev Reprod Toxicol* 77 (1):22-28.

Chen, W., Langer, R.M., Janczewska, S., Furian, L., Geary, R., Qu, X., Wang, M., Verani, R., Condon, T., Stecker, K., Bennett, C. F., and Stepkowski, S. M., (2005) Methoxyethyl-modified intercellular adhesion molecule-1 antisense phosphorothioate oligonucleotides inhibit allograft rejection, ischemic-reperfusion injury, and cyclosporine-induced nephrotoxicity, *Transplantation* 79 (4): 401-408.

Advani, R., Lum, B.L., Fisher, G.A., Halsey, J., Geary, R.S., Holmlund, J.T., Kwoh, T.J., Dorr, F.A., & Sikic, B.I. (2005) A phase I trial of aprinocarsen (ISIS 3521/LY900003), an antisense inhibitor of protein kinase C- $\alpha$  administered as a 24-hour weekly infusion schedule in patients with advanced cancer. *Invest New Drugs*, 23, 467-477.

Albertshofer, K., Siwkowski, A.M., Wanciewicz, E.V., Esau, C.C., Watanabe, T., Nishihara, K.C., Kinberger, G.A., Malik, L., Eldrup, A.B., Manoharan, M., Geary, R.S., Monia, B.P., Swayze, E.E., Griffey, R.H., Bennett, C.F. and A., M.M. (2005). "Structure-Activity Relationship Study on a Simple Cationic Peptide Motif for Cellular Delivery of Antisense Peptide Nucleic Acid." *J Med Chem.* 2005 Oct 20;48(21):6741-9.

Murphy, A.T., Brown-Augsburger, P., Yu, R.Z., Geary, R.S., Thibodeaux, S. and Ackermann, B.L. (2005). Development of an ion-pair reverse-phase liquid chromatographic/tandem mass spectrometry method for the determination of an 18-mer phosphorothioate oligonucleotide in mouse liver tissue. *Eur J Mass Spectrom (Chichester, Eng)* 11(2): 209-215.

Villalona-Calero, M.A., Ritch, P., Figueroa, J.A., Otterson, G.A., Belt, R., Dow, E., George, S., Leonardo, J., McCachren, S., Miller, G.L., Modiano, M., Valdivieso, M., Geary, R.S., Oliver, J.W. and Holmlund, J. (2004). A phase I/II study of LY900003, an Antisense inhibitor of protein kinase C- $\alpha$ , in combination with cisplatin and gemcitabine in patients with advanced non-small cell lung cancer. *Clin. Cancer Res.* 10(18 Pt 1): 6086-6093.

Yu, R.Z., Geary, R.S. and Levin, A.A. (2004). Application of novel quantitative bioanalytical methods for pharmacokinetic and pharmacokinetic/pharmacodynamic assessments of antisense oligonucleotides. *Curr Opin Drug Discov Devel* 7(2): 195-203.

Yu, R.Z., Geary, R.S., Monteith, D.K., Matson, J., Truong, L., Fitchett, J. and Levin, A.A. (2004). Tissue disposition of a 2'-O-(2-methoxy) ethyl modified antisense oligonucleotides in monkeys. *J. Pharm. Sci.* 93: 48-59.

Raof A.A., Chiu P, Ramtoola Z, Cumming I.K, Teng C, Weinbach S.P, Hardee G.E, Levin A.A, Geary R.S. (2004). Oral bioavailability and multiple dose tolerability of an antisense oligonucleotide tablet formulated with sodium caprate. *J Pharm Sci.*93: (6):1431-1439.

Geary, R.S., Yu, R.Z., Watanabe, T., Henry, S.P., Hardee, G.E., Chappell, A., Matson, J., Sasmor, H., Cummins, L. and Levin, A.A. (2003). Pharmacokinetics of a tumor necrosis factor- $\alpha$  phosphorothioate 2'-O-(2-methoxyethyl) modified antisense oligonucleotide: comparison across species. *Drug Metab. Dispos.* 31(11): 1419-1428.

Yu, R. Z., Su, J. Q., Grundy, J. S., Geary, R. S., Sewell, K. L., Dorr, A., and Levin, A. A. (2003). Prediction of clinical responses in a simulated phase III trial of Crohn's patients administered the antisense phosphorothioate oligonucleotide ISIS 2302: comparison of proposed dosing regimens. *Antisense and Nucleic Acid Drug Development* 13, 57-66.

Raof, A.A., Ramtoola, Z., McKenna, B., Yu, R.Z., Greg, H., Geary, R.S. Effect of sodium caprate on the intestinal absorption of two modified antisense oligonucleotide in pigs. *Eur J Pharm Sci*;17(3):131-138, 2002.

Cripps MC, Figueredo AT, Oza AM, Taylor MJ, Fields AL, Holmlund JT, McIntosh I.W, Geary RS, Eisenhauer EA. Phase II Randomized Study of ISIS 3521 and ISIS 5132 in Patients with Locally Advanced or Metastatic Colorectal Cancer: A National Cancer Institute of Canada Clinical Trials Group Study. *Clin Cancer Res*;8(7):2188-92, 2002.

Geary, R.S., Henry, S.P. and Grillone, L.R. Fomivirsen: Clinical Pharmacology and Potential Drug Interactions. *Drug Disposition.* 41(4):255-260, 2002.

Yu R.Z., Baker B., Chappell A., Geary R.S., Chueng E., Levin A.A. Development of an ultrasensitive noncompetitive hybridization-ligation enzyme-linked immunosorbent assay for the determination of phosphorothioate oligodeoxynucleotide in plasma. *Anal Biochem.* 304:19-25, 2002.

Cunningham CC, Holmlund JT, Geary RS, Kwoh TJ, Dorr A, Johnston JF, Monia B, Nemunaitis J. A Phase I trial of H-ras antisense oligonucleotide ISIS 2503 administered as a continuous intravenous infusion in patients with advanced carcinoma. *Cancer* 92(5):1265-71, 2001.

Henry, S.P., Geary, R.S., Yu, R., and Levin, A.A. Drug Properties of Second-Generation Antisense Oligonucleotides: How do They Measure Up to Their Predecessors. *Cur. Opin. Invest. Drugs.* 2(10):1444-1449, 2001.

Geary, R. S., Yu, R.Z., Levin, A.A. Pharmacokinetics of phosphorothioate antisense oligodeoxynucleotides. *Current Opinion in Investigational Drugs.* 2(4) :562-573, 2001.

Geary, R. S., Watanabe, T. A., Truong, L., Freier, S., Lesnik, E. A., Sioufi, N. B., Sasmor, H., Manoharan, M., and Levin, A. A. Pharmacokinetic properties of 2'-O-(2-methoxyethyl)-modified oligonucleotide analogs in rats. *J Pharmacol Exp Ther* 296(3):890-897, 2001.

Geary, R. S., Khatsenko, O., Bunker, K., Crooke, R., Moore, M., Burckin, T., Truong, L., Sasmor, H., and Levin, A. A. Absolute bioavailability of 2'-O-(2-methoxyethyl)-modified antisense oligonucleotides following intraduodenal instillation in rats. *J Pharmacol Exp Ther* 296(3):898-904, 2001.

Yu, R., Geary, R., Leeds, J., Watanabe, T., Moore, M., Fitchett, J., Matson, J., Burckin, T., Templin, M., and Levin, A. Comparison of pharmacokinetics and tissue disposition of an antisense phosphorothioate oligonucleotide targeting human Hla-ras mRNA in mouse and monkey. *J Pharm Sci* 90(2):182-193, 2001.

Yu, R. Z., Zhang, H., Geary, R. S., Graham, M., Masarjian, L., Lemonidis, K., Crooke, R., Dean, N. M., and Levin, A. A. Pharmacokinetics and pharmacodynamics of an antisense phosphorothioate oligonucleotide targeting Fas mRNA in mice. *J Pharmacol Exp Ther* 296(2):388-395, 2001.

Khatsenko, O., Morgan, R., Troung, L., York-Defalco, C., Sasmor, H., Conklin, B., Geary, R. Absorption of antisense oligonucleotides in rat intestine: effect of chemistry and length. *Antisense and Nucleic Acid Drug Dev.* 10(1):35-44, 2000.

Cunningham, C. C., Holmlund, J. T., Schiller, J. H., Geary, R. S., Kwoh, T. J., Dorr, A., and Nemunaitis, J. A phase I trial of c-ras kinase antisense oligonucleotide ISIS 5132 administered as a continuous intravenous infusion in patients with advanced cancer. *Clin Cancer Res* 6(5):1626-1631, 2000.

Leeds, J. M., Henry, S. P., Geary, R., Burckin, T., and Levin, A. A. Comparison of the pharmacokinetics of subcutaneous and intravenous administration of a phosphorothioate oligodeoxynucleotide in cynomolgus monkeys. *Antisense Nucleic Acid Drug Dev* 10(6):435-441, 2000.

Templin, M. V., Levin, A. A., Graham, M. J., Aberg, P. M., Axelsson, B. I., Butler, M., Geary, R. S., and Bennett, C. F. Pharmacokinetic and toxicity profile of a phosphorothioate oligonucleotide following inhalation delivery to lung in mice. *Antisense Nucleic Acid Drug Dev* 10(5):359-368, 2000.

Yuen, A. R., Halsey, J., Fisher, G. A., Holmlund, J. T., Geary, R. S., Kwoh, T. J., Dorr, A., and Sikic, B. I. Phase I study of an antisense oligonucleotide to protein kinase C- $\alpha$ . (ISIS 3521/CGP 64128A) in patients with cancer. Clin. Cancer Res. 5(11):3357-3363, 1999.

Nemunaitis, J., Holmlund, J. T., Kraynak, M., Richards, D., Bruce, J., Ognoskie, N., Kwoh, T. J., Geary, R., Dorr, A., Von Hoff, D., and Eckhardt, S. G. Phase I evaluation of ISIS 3521, an antisense oligodeoxynucleotide to protein kinase C- $\alpha$ , in patients with advanced cancer. J. Clin. Oncol. 17(11):3586-3595, 1999.

Geary, R.S., Matson, J., and Levin, A.A. A Nonradioisotope Biomedical Assay for Intact Oligonucleotide and Its Chain-Shortened Metabolites Used for Determination of Exposure and Elimination Half-Life of Antisense Drugs in Tissue. Anal. Biochem. 274: 241-248, 1999.

Yu, R.Z., Geary, R.S., Leeds, J.M., Watanabe, T., Fitchett, J.R., Matson, J.E., Mehta, R., Hardee, G.R., Templin, M.V., Huang, K., Newman, M.S., Quinn, Y., Uster, P., Zhu, G., Working, P.K., Horner, M., Nelson, J., and Levin, A.A. Pharmacokinetics and tissue disposition in monkeys of an antisense oligonucleotide inhibitor of Ha-Ras encapsulated in stealth liposomes. Pharm. Res. 16 (8): 1309-1315, 1999.

Monteith, D.K., Horner, M.J., Gillett, N.A., Butler, M., Geary, R., Burckin, T., Ushiro-Watanabe, T., and Levin, A. Evaluation of the renal effects of an antisense phosphorothioate oligodeoxynucleotide in monkeys. Toxicologic Pathology. 27 (3): 307-317, 1999.

Monteith, D.K., Geary, R.S., Johnston, J., Monia, B.P., Levin, A. Preclinical evaluation of the effects of a novel antisense compound targeting C-raf kinase in mice and monkeys. Toxicol Sci. 46(2):365-375, 1998.

Ramanathan, R., Geary, R.S., Bourne, D.W., and Putcha, L. Bioavailability of intranasal promethazine dosage forms in dogs. Pharmacol. Res. 38 (1): 35-39, 1998.

Phillips, J.A., Craig, S.J., Bayley, D., Christian, R.A., Geary, R. and Nicklin, P.L. Pharmacokinetics, metabolism, and elimination of a 20-mer phosphorothioate oligodeoxynucleotide (CGP 69846A) after intravenous and subcutaneous administration. Biochem. Pharmacol. 54(6): 657-668, 1997.

Glover, J.M., Leeds, J.M., Mant, T.G.K., Amin, D., Kisner, D. L., Zuckerman, J. E., Geary, R.S., Levin, A. A. and Shanahan, Jr., W.R. Phase I safety and pharmacokinetic profile of an intercellular adhesion molecule-1 antisense oligodeoxynucleotide (ISIS 2302). J. Pharmacol. Exp. Ther. 282(3): 1173-1180, 1997.

Leeds, J.M., Geary, R.S., Henry, S.P., Glover, J., Shanahan, W., Fitchett, J., Burckin, T., Truong, L., and Levin, A.A. Pharmacokinetic properties of phosphorothioate oligonucleotides. IRT: Nucleosides and Nucleotides, 16: 1689-1693, 1997.



Geary, R.S., Leeds, J.M., Henry, S.P., Monteith, D.K. and Levin, A.A. Antisense oligonucleotide inhibitors for the treatment of cancer: 1. Pharmacokinetic properties of phosphorothioate oligodeoxynucleotides. *Anti-Cancer Drug Design* 12(5): 383-393, 1997.

Geary, R.S., Leeds, J.M., Fitchett, J., Burckin, T., Truong, L., Spainhour, C., Creek, M. and Levin, A.A. Pharmacokinetics and metabolism in mice of a phosphorothioate oligonucleotide antisense inhibitor of C-rf-1 kinase expression. *Drug Metabolism and Disposition* 25(11): 1272-1281, 1997.

Weiss, D.J., Geary, R.S., Wustenberg, W., Bucci, T.J., Perman, V., Baumel, I.P. and Dacre, J.C. The comparative metabolism of diisopropyl methylphosphonate in mink and rats. *Arch. Environ. Contam. Toxicol.* 27(3): 420-5, 1994.

Geary, R.S. and Schlameus, H.W. Vancomycin and insulin used as models for oral delivery of peptides. *J. Controlled Release* 23(1): 65-74, 1993.

Geary, R. and Stavchansky, S. Gas-liquid chromatographic determination of almitrine in rat intestinal fluid using flame ionization detection. *Anal. Lett.* 25(10): 1843-50, 1992.

Miller, M.A. and Geary, R.S. RIA-linked microdialysis sampling in the awake rat: application to free-drug pharmacokinetics of hydrocortisone. *J. Pharm. Biomed. Anal.* 9(10-12): 901-10, 1991.

Geary, R.S., Swynnerton, N.F., Timmons, S.F. and Mangold, D.J. Characterization of WR-1065 absorption in the rat small intestine. *Biopharm. Drug Dispos.* 12(4): 275-84, 1991.

Mangold, D.J., Huelle, B.K., Miller, M.A., Geary, R.S., Sanchez-Barona, D.O.T., Swynnerton, N.F., Fleckenstein, L. and Ludden, T.M. Pharmacokinetics and disposition of WR-1065 in the rhesus monkey. *Drug Metabolism and Disposition* 18(3): 281-287, 1990.

Stavchansky, S., Doluisio, J.T., MacLeod, C.M., Szalkowski, M.B., Bachand, Jr., R.T., Heilman, R., Sebree, T.B. and Geary, R.S. Single oral dose proportionality pharmacokinetics of almitrine bismesylate in humans. *Biopharm. Drug Dispos.* 10(3): 229-37, 1989.

Stavchansky, S., Doluisio, J.T., MacLeod, C.M., Sebree, T.B., Heilman, R., Bachand, Jr., R.T., Szalkowski, M.B. and Geary, R.S. Relative bioavailability of almitrine bismesylate in humans. *Biopharm. Drug Dispos.* 10(3): 239-46, 1989.

Geary, R.S., Swynnerton, N.F., Miller, M.A., Mangold, D.J. and Ludden, T. Intraduodenal administration of ethiofos (WR-2721): dose proportionality study in the rhesus monkey. *Res. Commun. Chem. Pathol. Pharmacol.* 65(2): 147-59, 1989.

Coleman, M.D., Fleckenstein, L., Geary, R.S., Brewer, T.G., Timony, G.A. and Mangold, D.J. The disposition of ethiofos (WR-2721) in the isolated perfused rat liver. *Radiat. Res.* 117(2): 334-41, 1989.

Stavchansky, S., Wallace, J.E., Geary, R., Hecht, G., Robb, C.A. and Wu, P. Bioequivalence and pharmacokinetic profile of promethazine hydrochloride suppositories in humans. *J. Pharm. Sci.* 76(6): 441-5, 1987.

Stavchansky, S., Eghbali, B. and Geary, R. Stability indicating assay of lidocaine hydrochloride in solution. *Anal. Lett.* 20(5): 821-7, 1987.

Stavchansky, S., Riffée, W. and Geary, R.S. Chronic administration of phenylpropanolamine and caffeine: effect on locomotor activity. *Res. Commun. Subst. Abuse* 7(1-2): 37-48, 1986.

Stavchansky, S., Riffée, W. and Geary, R. Comparison between locomotor activity changes produced by phencyclidine and d-amphetamine in CD-1 male mice. *Res. Commun. Chem. Pathol. Pharmacol.* 48(2): 189-202, 1985.

### **ABSTRACTS AND PRESENTATIONS:**

M.R. Hodges, MB BS, BSc, E. Castelleo, MD, A. Chen, MA, R.S. Geary, PhD, J.G. Karras, PhD, D. Shapiro, MB BS, B. Yeung, BSc, R. Yu, PhD, S.A. Gregory, PhD. Randomized, Double-Blind, Placebo Controlled First in Human Study of Inhaled AIR645, an IL-4R Oligonucleotide, in Healthy Volunteers. Presented at ATS, San Diego, CA, May 18, 2009. Published 4/24/09 on ATS website.

Fey RA<sup>1</sup>, Geary RS<sup>1</sup>, Norris DA<sup>1</sup>, Boyd RB<sup>2</sup> and Henry SP<sup>1</sup>. 1: Isis Pharmaceuticals, Inc. 2: Northern Biomedical Research. Pharmacokinetics of an Antisense Oligonucleotide Administered as a Continuous Intrathecal Infusion in Monkey. Presented at 58th Annual SOT Meeting and ToxExpo, Baltimore Convention Center, Baltimore, MD. March 15-18, 2009.

Norris DA, Matson J, and Geary RS. Comparison of the Pharmacokinetics of a C-Reactive Protein Antisense Oligonucleotide, ISIS 353512, in Rats and Monkeys after 3-months of Dosing. Presented at AAPS Annual Meeting, Atlanta, GA, November 16-20, 2008.

Baek MS, Yu R, Gaus H and Geary RS. In vitro metabolism of Mipomersen (ISIS 301012), a second-generation antisense oligonucleotide targeting human apoB-100. Presented at AAPS Annual Meeting, Atlanta, GA, November 16-20, 2008.

Geary, RS. Pharmacokinetics of Antisense Oligonucleotides: Relationship to Safety and Pharmacology. Oral presentation at American College of Toxicology Annual Meeting, Tucson, AZ, November 9-12, 2008.

Geary, RS. Pioneering RNA-based Drug Discovery & Development. Oral presentation at BIOCOM Investor Conference, La Jolla, CA, October 28, 2008.

Geary, RS. Bioanalytical Issues and Applications for Antisense Oligonucleotide Development: From Bench to Bedside. Oral presentation at DIA, Washington DC, September 22-24, 2008.

Watanabe T, Riley G, Kuller A, and Geary RS. In Vitro Protein Binding Evaluation of an Antisense Oligonucleotide, Mipomersen, Targeting Human Apolipoprotein B-100. Presented at AAPS National Biotechnology Conference, Toronto, Canada, June 22-25, 2008.

Geary RS, Pearce M, Wanciewicz E, Hung G, Henry SP, Matson J, Crosby J, Karras J, Gregory S, and Yu RZ. Pharmacokinetic and Pharmacodynamic Effects of 2'-MOE Partially Modified Phosphorothioate Antisense Oligonucleotides Administered Directly to Lung and Cerebrospinal Fluid. Presented at Society of Toxicology 47th Annual Meeting & ToxExpo, Seattle, WA, March 16-20, 2008.

Yu RZ, Geary RS, Kim TW, and Levin A. Mouse and Monkey Toxicokinetics of a Second Generation Antisense Oligonucleotide (ASO) Targeting Human ApoB-100, following Chronic Treatment for up to 1 Year. Presented at AAPS Annual Meeting & Expo, San Diego, CA, November 10-15, 2007.

Watanabe T, Riley G and Geary RS. In Vitro Protein Binding Evaluation and Drug Interaction Studies of an Antisense Oligonucleotide, ISIS 325568, Targeting Glucagon Receptor (GCGR). Presented at AAPS Annual Meeting & Expo, San Diego, CA, November 10-15, 2007.

Yu RZ, Crosby J, Pearce M, Matson J, Gregory S and Geary RS. Pharmacokinetic, Tissue Disposition and Excretion of 2'-MOE Partially Modified Phosphorothioate Antisense Oligonucleotide, Targeting IL-4Ra, Following Aerosol Inhalation in Mice. Presented at AAPS National Biotechnology Conference in San Diego, CA, June 24-27, 2007.

Watanabe T, Matson J and Geary RS. Mass Balance ADME Rat Study of (3H)-ISIS 325568, a 2'-Methoxyethyl (MOE) Modified Antisense Oligonucleotide (ASO) Targeting Human Glucagon Receptor. Presented at AAPS National Biotechnology Conference, San Diego, June 24-27, 2007.

Wanciewicz E, Siwkowski A, Meibohm B, Yates C, Pearce M, Matson J, Chew N, Lillie C, Tillman L, Hung G, Geary RS, Bhanot S and Monia B. Short (12-Nucleotide) 2nd Generation Antisense Oligonucleotides Selectively Inhibit SGLT2 mRNA Expression Across Multiple Species and Are Bioavailable Following Intrajeunal Administration. Presented at American Diabetes Association (ADA) 67th Scientific Sessions, Chicago, IL, June 22 - 26, 2007.

Geary RS, Pearce M, Wanciewicz E, Hung G, Henry S, Matson J, Crosby J, Karras J, Gregory S and Yu RZ. Pharmacokinetic and Pharmacodynamic Effects of 2'-MOE Partially Modified Phosphorothioate Antisense Oligonucleotides Administered Directly to Lung and Cerebrospinal Fluid. Presented at Society of Toxicology 46th Annual Meeting & ToxExpo, Charlotte, NC, March 25-29, 2007.

Stein E, Flaim J, Chuang E, Wedel M, Su J, Geary RS, Yu R, Kastelein J. Statin-Like Dose-Dependent Reductions in LDL-C and Apolipoprotein B with ISIS 301012 - An Antisense Inhibitor of ApoB in Subjects with Polygenic Hypercholesterolemia. Presented at ACC 56<sup>th</sup> Annual Scientific Session, New Orleans, LA, March 24-27, 2007.

Geary RS, Siwkowski A, Matson J, Watanabe T, Henry S and Levin A. *In Vivo* Pharmacokinetic / Pharmacodynamics of Backbone Modified 2'-MOE Antisense Oligonucleotides (ASO) in Rodents. Presented at the 40<sup>th</sup> Society of Toxicology Annual Meeting, San Diego, CA, March 5-9, 2007.

Geary RS, Pearce M, Wanciewicz E, Hung G, Henry S, Matson J, Crosby J, Karras J, Gregory S and Yu RZ. Pharmacokinetic and Pharmacodynamic Effects of 2'-MOE Partially Modified Phosphorothioate Antisense Oligonucleotides Administered Directly to Lung and Cerebrospinal Fluid. Presented at the 40<sup>th</sup> Society of Toxicology Annual Meeting, San Diego, CA, March 5-9, 2007.

Kastelein, J., Bradley, J., Chuang, E., Wedel, M., Su, J., Geary, R., Yu, R., Effect of Dose and Dose Schedule on the Efficacy and Safety of an Antisense Inhibitor of APOB in Volunteers with Mild Hypercholesterolemia, Presented at the XIV International Symposium on Atherosclerosis, Rome, Italy, June 18-22, 2006.

Geary, R., Yu, R., Bradley, J., Chuang, E., Wedel, M., vanVliet, A., Lack of Pharmacokinetic Interaction of an Antisense Oligonucleotide, Targeting Human APOB, When Coadministered with Simvastatin and Ezetimibe in Man, Presented at the XIV International Symposium on Atherosclerosis, Rome, Italy, June 18-22, 2006.

Geary, R.S ADME Strategies for Accelerating Preclinical Development of Antisense Oligonucleotides. Presented at the Strategic Research Institute Conference – Preclinical Development, La Jolla, CA, 2005.

Geary, R.S., Application of Novel Bioanalytical Methods for Pharmacokinetics and PK/PD Assessments of Antisense Oligonucleotides Presented at the EuroTIDES Conference, Berlin, Germany, 2003.

Nishihara, K.C., Grundy, J.J., Kim, J., Geary, R.S. and Watanabe, T.A. Pharmacokinetics Of 2'-methoxyethyl (2'-MOE) Oligonucleotide Endonuclease Metabolites In Rats. Presented at the AAPS Annual Meeting and Exposition, Salt Lake City, UT, 2003.

Vick, A., Geary, R.S., Henry, S.P., Rinkema, L. and Reddy, V. Comparative Pharmacokinetics And Metabolism Of A 20-mer Oligodeoxynucleotide Phosphorothioate (affinitak) In Mice And Cynomolgus Monkeys Following Intravenous Administration. Presented at the AAPS Annual Meeting and Exposition, Salt Lake City, UT, 2003.

Yu, R.Z., Riley, G., Hoc, K., Watanabe, T.A., Matson, J., Murray, S., Booten, S., Bhanot, S., Monia, B. and Geary, R.S. Effect Of Treatment Regimen On Sub-organ Pharmacodynamics Of A 2'-moe Modified Antisense Oligonucleotide, Isis 116847, Targeting Putative Protein Tyrosine Phosphatase (pten) Mrna In Rats. Presented at the AAPS Annual Meeting and Exposition, Salt Lake City, UT, 2003.

Geary, Richard S., Current assessment of PK/PD relationships for antisense therapeutics. Presented at the World congress of Pharmacy and pharmaceutical Sciences, Nice, France, 2002. (Abstract)

Pacheco, G., Henry, S., Geary, R., and De Peyster, A. Characterization of Nonspecific Effects of Phosphorothioate Antisense Oligodeoxynucleotides on Cytochrome P450 3A2 and Cytochrome P450 2C11 in Male Sprague-Dawley Rats. Presented at the Annual Meeting of the Society of Toxicology, Nashville, TN, 2002. (Abstract)

Yu, Rosie Z., Matson, John, and Geary, Richard S. Terminal Elimination Rates for Antisense Oligonucleotides in Plasma Correlate with Tissue Clearance Rates in Mice and Monkeys. Presented at the Annual Meeting of the American Association of Pharmaceutical Scientists, Denver, CO, 2001. (Abstract)

Cummins, Len, Geary, Richard S., Watanabe, Tanya, Chappell, Alfred, Matson, John, and Levin, Arthur A. Metabolism Characteristics of a Modified Antisense Oligonucleotide, ISIS 104838. Presented at the Annual Meeting of the American Association of Pharmaceutical Scientists, Denver, CO, 2001. (Abstract)

Watanabe, T.A., Geary, R.S., and Levin, A.A. In Vitro Plasma Protein Binding of Antisense Oligonucleotides: Effects of Chemistry and Length. Presented at the Annual Meeting of the American Association of Pharmaceutical Scientists, Denver, CO, 2001. (Abstract)

Gibiansky, L., Gibiansky, E., Yu, R.Z., and Geary, R.S. (2001) ISIS 2302: Validation of the Population PK Model and PK/PD Analysis. Presented at the Annual Meeting of the American Association of Pharmaceutical Scientists, Denver, CO, 2001. (Abstract)

Henry, Scott P, Geary, Richard, Yu, Rosie, Templin, Mike V, Pallman, Jeff  
Levin, Arthur (2001) Comparison of toxicity and tissue concentrations for 1st and 2nd generation antisense oligonucleotide. Society Of Toxicology, San Francisco, CA, P.325. (Abs 1543)

Geary, Richard, Mathison, Brian, Watanabe, Tanya, Savides, Michael C, Henry, Scott P, Levin, Arthur A. (2001) Second generation antisense oligonucleotide pharmacokinetics and mass balance following intravenous administration in rats. Society Of Toxicology, San Francisco, CA, P.343. (Abs 1633)

Stepkowski, S. M., Chen, W., Geary, R., Wang, M. E., Condon, T., Stecker, K., and Bennett, C. F. (2001). Development of an oral formulation for ICAM-1 antisense oligonucleotides. Transplant Proc. 33 (1-2):387, 2001.

Stepkowski, S. M., Chen, W., Geary, R. S., Wang, M. E., Condon, T., Stecker, K., and Bennett, C. F. (2001). An oral formulation for intracellular adhesion molecules-1 antisense oligonucleotides. Transplant Proc 33. (Abs 3271)

Geary, R.S., Chappell, A., Teng, C., Erwin, R., Kornburst, D. and Hardee, G.E. (2000). Plasma bioavailability and tolerability of antisense oligonucleotides following intrajejunal (IJ)

administration with absorption enhancers in conscious rhesus monkeys. Presented at the Annual Meeting of the American Association of Pharmaceutical Scientists, Indianapolis, IN, October 29 – November 2, 2000, P.216. (Abs 3295)

Geary, R.S., Thuong, L., Weinbech, S., Teng, C., Tillman, L.G., Perry, B.A., Sinko, P.J., and Hardee, G.E. (2000). Intestinal site of absorption and tolerability of formulated 2'-O-methoxyethyl (MOE) modified antisense oligonucleotide in a conscious dog model. Presented at the Annual Meeting of the American Association of Pharmaceutical Scientists, Indianapolis, IN, October 29 – November 2, 2000, P.216. (Abs 3294)

Geary, R.S., Teng, C., Raoof, A.A., Ramtoola, Z., and Hardee, G.E. (2000). Cross-species comparison of the tolerability and effect of absorption enhancer on systemic delivery of antisense oligonucleotide s following intra-intestinal administration. Presented at the Annual Meeting of the American Association of Pharmaceutical Scientists, Indianapolis, IN, October 29 – November 2, 2000, P.216. (Abs 3293)

Tillman, L.G., Geary, R.S., Pan, Y., Teng, C., Lin, D. and Hardee, G.E. (2000). In vitro and in vivo performance and tolerability in dogs of antisense oligonucleotide tablets formulated with permeation enhancers. Presented at the Annual Meeting of the American Association of Pharmaceutical Scientists, Indianapolis, IN, October 29 – November 2, 2000, P.216. (Abs 3111)

Cho, M., Geary, R.S., and Stavchansky, S. (2000). Renal uptake and clearance of an antisense oligonucleotide (ISIS 2105) in the in situ perfused rat kidney. Presented at the Annual Meeting of the American Association of Pharmaceutical Scientists, Indianapolis, IN, October 29 – November 2, 2000, P.216. (Abs 1235)

Stavchansky, S., Geary, R.S., and Cho, M. (2000). Pharmacokinetics and hepatic first pass effect of an antisense oligonucleotide (ISIS 2302) in rats. Presented at the Annual Meeting of the American Association of Pharmaceutical Scientists, Indianapolis, IN, October 29 – November 2, 2000, P.216. (Abs 1233)

Yu, R., Zhang, H., Geary, R.S., Graham, M., Masarjian, L., Lemonidis, K., Crooke, R., Dean, N., and Levin, A.A. (2000). Pharmacokinetics and pharmacodynamics of an antisense phosphorothioate oligonucleotide targeting Fas mRNA in mice. Presented at the Annual Meeting of the American Association of Pharmaceutical Scientists, Indianapolis, IN, October 29 – November 2, 2000, P.216. (Abs 2644)

Adjei, A.A., Erlichman, C., Sloan, J.A., Hanson, L.J., Reid, J., Atherton, P., Geary, R., Holmlund, J., and Dorr, A., (2000). A phase I trial of ISIS 2503, an antisense inhibitor of H-ras in combination with gemcitabine in patients with advanced cancer. Presented at the Annual Meeting of the American Society of Clinical Oncology, New Orleans, LA, May 2000, 19: 186a. (Abs 722)

Advani, R., Fisher, G.A., Lum, Bert L., Halsey, J., Yuen, A., Holmlund, J.T., Kwok, T.J., Dorr, A., Geary, R., Sikic, B.I., (2000). Coagulation and complement effects of antisense phosphorothioate oligonucleotide targeting protein kinase C-? (ISIS 3521) are schedule and dose

dependent. Presented at the Annual Meeting of the American Society of Clinical Oncology, New Orleans, LA, May 2000, 19: 208a. (Abs 809)

Yuen, A., Advani, R., Fisher, G., Halsey, J., Lum, B., Geary, R., Kwok, T.J., Dorr, A., Sikic, B.I., (2000). A phase I/II trial of ISIS 3521, an antisense inhibitor of protein kinase C alpha, combined with carboplatin and paclitaxel in patients with non-small cell lung cancer. Presented at the Annual Meeting of the American Society of Clinical Oncology, New Orleans, LA, May 2000, 19: 459a. (Abs 1802)

Soucy, N.V., Riley, J.P., Templin, M.V., Geary, R.S., (2000). Maternal and fetal disposition of a phosphorothioate oligonucleotide, 3H-ISIS 2105, following 3-hour or 7-day intravenous infusion to pregnant rats. Presented at 39th Annual Meeting of the Society of Toxicology, Philadelphia, PA, March 2000, 54(1): 58. (Abs 269)

Geary, R.S., (1999). Antisense Technology: New Applications. Presented at the 1999 AAPS Annual Meeting, New Orleans, LA, American Association of Pharmaceutical Scientists.

Geary, R.S., Morgan, R., Truong, L., Bunker, K., Fitchett, J., Freier, S., Sioufi, N., Lesnik, E. and Manoharan, M., (1999). Pharmacokinetic properties of 2'-Methoxyethyl Ribose modified antisense oligonucleotides in rats. Presented at the 1999 AAPS Annual Meeting, New Orleans, LA, American Association of Pharmaceutical Scientists.

Khatsenko, O., Guzaev, A., Bhat, B., Morgan, R., Soucy, N., Manoharan, M. and Geary, R.S. (1999). Conjugation with folic acid improves oral bioavailability of phosphorothioate oligonucleotide. Presented at the 1999 AAPS Annual Meeting, New Orleans, LA, American Association of Pharmaceutical Scientists.

Watanabe, T.A., Lesnik, E., Freier, S., Sioufi, N. and Geary, R.S., (1999). Whole plasma and human serum albumin binding capacity, affinity and interactions of antisense phosphorothioate oligonucleotides across sequence (ISIS 2302, 2503, 3521, and 5132). Presented at the 1999 AAPS Annual Meeting, New Orleans, LA, American Association of Pharmaceutical Scientists.

Yu, R.Z., Baker, B., Chappell, A., Truong, L., Cheung, E., Geary, R.S. and Levin, A.A., (1999). Development of an Ultra-Sensitive Elisa Assay for the determination of phosphorothioate oligodeoxynucleotide in plasma. Presented at the 1999 AAPS Annual Meeting, New Orleans, LA, American Association of Pharmaceutical Scientists.

Geary, R.S., Yu, R., Henry S.P. and Levin, A.A., (1999). Cross-species pharmacokinetics comparison of an ICAM-1 antisense oligonucleotide, ISIS 2302, from mouse to man, Presented at 38th Annual Meeting of the Society of Toxicology, March 1999, 48 (1-S): 209.

Geary, R., Morgan, R., Fitchett, J., Winniman, M., Manoharan, M., and Guzaev, A., (1999). Comparison of the Pharmacokinetic Profile of a [3H] Cholesterol [3H]-Conjugated and -Unconjugated P=O MOE, Presented at 38th Annual Meeting of the Society of Toxicology, March 1999, 48, (1-S): 174.

Jagels, M., Henry, S., Hugli, T., Geary, R. Levin, A., (1999). In Vitro Model for Investigation of Complement Activation by a Phosphorothioate Oligodeoxy-Nucleotide  
Presented at 38th Annual Meeting of the Society of Toxicology, March 1999, 48, (1-S): 68.

Monteith, D., Geary, R., Henry, S., Templin, M., and Levin, A., (1999). Antisense oligonucleotides: Toxicology from Mice to Humans, Presented at 38th Annual Meeting of the Society of Toxicology, March 1999, 48, (1-S): 39.

Sandler, A., Gordon, M.S., Holmlund, J.T., Dorr, A., Battiato, L., Fife, K., Geary, R., Kwok, T.J., and Sledge G.W., (1999). A phase 1 trial of ISIS 2503, an antisense inhibitor of H-Ras, administered by a 24-hour weekly infusion to patients with advanced cancer.  
American Society of Clinical Oncology Annual Meeting, 1999.

Geary, R.S., (1998). Antisense Oligonucleotide pharmacokinetics and metabolism: cross-species scaling to clinical experience. Annual Symposium on Biotechnology, Tahoe City, CA.

Geary, R.S., (1998). Oral delivery and pharmacokinetics of antisense oligonucleotides. CHI's Antisense Technologies, San Francisco, CA.

Geary, R.S., Troung, L., Morgan, R., Ushiro-Watanabe, T. and Monia, B.P., (1998). Comparative pharmacokinetics, biodistribution and metabolism of two PKC antisense oligonucleotides in rats. 1998 AAPS Annual Meeting, San Francisco, CA, American Association of Pharmaceutical Scientists.

Hanson, G., Kolbe, P., Rahavendran, S.V., Geary, R. and Leeds, J., (1998). Validation of a method for the measurement of ISIS 2302 and metabolites (N-1, N-2, N-3, N-4) human and dog plasma using capillary gel electrophoresis with ultraviolet detection. 1998 AAPS Annual Meeting, San Francisco, CA, American Association of Pharmaceutical Scientists.

Hardee, G.E., Mehta, R., Geary, R.S., Tillman, L., Khatsenko, O., Templin, M., Teng, C.L., Bennett, F. and Levin, A., (1998). The pharmacokinetics and toxicity of oligonucleotides: New routes of administration. 1998 AAPS Annual Meeting, San Francisco, CA, American Association of Pharmaceutical Scientists.

Khatsenko, O., Morgan, R. and Geary, R.S., (1998). Effect of oligonucleotide size and chemistry on intestinal absorption in an in situ rat model. 1998 AAPS Annual Meeting Abstracts, San Francisco, CA, American Association of Pharmaceutical Scientists.

Sikic, G.E., Yuen, A.R., Fisher, J., Pribble, G.A., Smith, J.P., Geary, R.S. and Dorr, A., (1998). A phase I trial of an antisense oligonucleotide targeted to protein kinase C- $\alpha$  (ISIS 3521) delivered by twenty-one day continuous infusion. 33rd Annual Meeting of the American Society of Clinical Oncology, Denver, CO.

Yu, R.Z., Geary, R.S., Monteith, D.K., Troung, L., Matson, J., Burckin, T., Fitchett, J., Leeds, J.M. and Levin, A.A., (1998). Plasma and tissue disposition of a 2'-methoxyethyl



modified antisense oligonucleotide targeting human C-raf kinase in cynomolgus monkeys. 1998 AAPS Annual Meeting, San Francisco, CA, American Association of Pharmaceutical Scientists.

Geary, R.S. and Miller, M.A. (1997). Chemical methods development for quantitation of phytochemicals in aqueous garlic extract. *Nutraceuticals: Des. Foods III: Garlic, Soy Licorice, [Course Des. Foods, Proc.]*, 3rd, Food & Nutrition Press, Trumbull, Conn.

Geary, R.S., Henry, S.P., Monteith, D.K., Leeds, J.M., Yu, R., Levin, A.A., (1997) Similarity and Differences of Interspecies exposure for antisense oligodeoxynucleotides. Presented at the Nature Biotechnology Antisense Conference: Antisense 97: Targeting the Molecular Basis of Disease, May 1997.

Geary, R.S., Howard, R., Trent, K., Cooper, S., Teng, C.L., Bunker, K., Lin, D., Cummins, L., Sasmor, H., Phillips, J., Bennett, F., (1997). Oral bioavailability of unmodified and modified oligonucleotides. Presented at the Nature Biotechnology Antisense Conference: Antisense 97: Targeting the Molecular Basis of Disease, May 1997.

Geary, R.S., Leeds, J.M., Fitchett, J., Ferdinandi, E., and Levin, A.A., (1997). Pharmacokinetics, tissue distribution and excretion of an antisense phosphorothioate oligonucleotide, ISIS 3521 (CGP 69846A), in rats: IV bolus vs. continuous IV infusion. Presented at the Society of Toxicology Annual Meeting, Cincinnati, OH. March, 1997.

Pallman, J., Ackerman, L., Monteith, D.K., Geary, R.S., and Spainhour, C.B., (1997). The toxicities in mice of a novel antisense compound targeting C-raf kinase. Presented at the Society of Toxicology Annual Meeting, Cincinnati, OH, March 1997.

Leeds, J.M., Kiorpes, A., Geary, R., Henry, S.P., Goldensoph, C., and Levin, A.A., (1996) Single dose subcutaneous bioavailability of ISIS 2302, a phosphorothioate oligonucleotide, in cynomolgus monkeys. Presented at the American Association of Pharmaceutical Scientists Annual Meeting and Exposition, Seattle, WA, November 1996.

Geary, R.S., Leeds, J.M., Shanahan, W., Glover, J., Pribble, J., Truong, L., Fitchett, J., Burckin, T., Nicklin, P. and Levin, A.A., (1996) Sequence independent plasma and tissue pharmacokinetics for 3 antisense phosphorothioate oligonucleotides: mouse to man. Presented at the American Association of Pharmaceutical Scientists, Annual Meeting of Exposition, Seattle, WA, November 1996.

Monteith, D.K., Geary, R.S., Spainhour, C.B., Ackerman, L., Monia, B.P., (1996) The effects in mice of a novel antisense compound targeting C-Raf Kinase. Geary, R.S., Spainhour, C.B., Ackerman, L., Monia, B.P. Presented at the XII International Roundtable -- Nucleosides, Nucleotides and Their Biological Applications. La Jolla, CA, September 1996.

Leeds, J.M., Geary, R.S., Henry, S.P., Monteith, D., Fitchett, J., Truong, L., Levin, A., (1996) Pharmacokinetic properties of phosphorothioate oligonucleotides. Presented at the XII International Roundtable -- Nucleosides, Nucleotides and Their Biological Applications. La Jolla, CA, September 1996.

Geary, R.S., Leeds, J.M., Henry, S.P., Montieth, D.K., Truong, L., Fitchett, J., Burckin, T., (1996) Analysis of subchronic exposure and toxicity across species for phosphorothioate oligonucleotides. Presented at the XII International Roundtable -- Nucleosides, Nucleotides and Their Biological Applications. La Jolla, CA, September 1996.

Baron, D., Burton, E.G. and Geary, R.S., (1996) Pharmacodynamic assessment of recombinant human tissue factor pathway inhibitor (tfpi) in the conscious baboon. *The Toxicologist* 1996, 30 (1), Part 2.

Chaturvedi, P., Geary, R.S., Harding, M., Schmalbach, T., (1995). Evaluation of the pharmacokinetic interaction between VX-710 and paclitaxel (TAXOL®) in beagle dogs. Presented at the American Association of Pharmaceutical Scientists, 10th Annual Meeting and Exposition, Miami Beach, FL, November 1995.

Chaturvedi, P. and Geary, R.S., (1995). Intravenous bolus pharmacokinetics of VX-710 in beagle dogs. Presented at the American Association of Pharmaceutical Scientists, 10th Annual Meeting and Exposition, Miami Beach, FL, November 1995.

Geary, R.S. and Miller, M.A., (1994). Chemical methods development for quantitation of phytochemicals in aqueous garlic extract. Presented at the designer foods iii, "phytochemicals in garlic, soy, licorice research update and implications", May 23-25, 1994, Georgetown University Conference Center, Washington, D.C.

Geary, R.S., (1994) A novel drug delivery system. Presented at the Dual-Use Space Technology Transfer Conference, NASA Johnson Space Center, Houston, TX, February 2, 1994.

Orr, J.L., Geary, R.S. and Miller, M.A., (1993). Physiologically based pharmacokinetic models and rational acute neurotoxicity test planning. *The Toxicologist*, 1993, 13, 246.

Barchfeld, G.L., Mason, O.B., Valensi, J.P., Schlameus, H.W., Geary, R.S., Van Nest, G., (1993). Serum and mucosal antibody responses to parenteral oral mucosal subunit vaccines in animal models. Presented at the novel Vaccine Strategies Mucosal Immunization, Adjuvants & Genetic Approach Meeting, Bethesda, MD, October 6-8, 1993.

Geary, R.S., Wustenberg, W., Weiss, D., Perman, V., Wall, C., Timmons, S.F., Bucci, T., Dacre, J., and Baumel, I., (1992). Quantification and identification of diisopropylmethylphosphonic acid and its primary metabolite, isopropylmethylphosphonic acid, in mink and rat. Presented at the American Association of Pharmaceutical Scientists, 7th Annual Meeting and Exposition, San Antonio, TX, November 1992.

Geary, R.S., Miller, M.A., Wustenberg, W., Bucci, T.J., Dacre, J.C., Baumel, I., Weiss, D.J., and Perman, V., (1992). Comparative pharmacokinetics and metabolism of diisopropyl-methylphosphonic acid (DIMP) in rat and mink. Fourth North American ISSX Meeting, Bal Harbour, FL, November 5, 1992.

Geary, R.S. and Schlameus, W., (1992) Bioavailability and nonparenteral dosage formulation for models of recombinant cytokines. Presented at the Biomaterials Bioassessment Initiative Mini Symposium and Poster Session at the Texas Research Park's Pawel Conference Center and Research Plaza I, San Antonio, TX, March 20, 1992.

Miller, M.A. and Geary, R.S., (1991) Effect of protein binding on free-drug pharmacokinetics as determined by RIA-linked microdialysis in the awake rat. Presented at the 3rd International Symposium on Pharmaceutical and Biomedical Analysis, Boston, MA, April 28-May 1, 1991.

Geary, R.S., Timmons, S.F., and Schlameus, H.W., (1990). Bioavailability and pharmacokinetics of some selected biological response modifiers: a synthetic glycolipid (s-TDCM) and a water-soluble yeast extract. Proceedings of the Fourth Annual Meeting of the American Association of Pharmaceutical Scientists, Pharm. Res., 1990, 7(9), S-276.

Geary, R.S., Timmons, S.F., and Mangold, D.J., (1989). In situ absorption of ethiofos and WR-1065: effects of buffer and absorption enhancers. Proceedings of the Fourth Annual Meeting of the American Association of Pharmaceutical Scientists, Pharm. Res. 1989, 6(9), S-230.

Swynnerton, N.F. and Ludden, T.M., (1988). Disposition of WR-1065 in the rhesus monkey. Proceedings of the Third Annual Meeting of the American Association of Pharmaceutical Scientists, Pharm. Res. 1988, 5(10), S-205.

Geary, R.S., Goldzieher, J.W., Doluisio, J.T., Newberger, J. and Mangold, D.J., (1988). Pharmacokinetics and relative bioequivalence of sustained-release steroid formulations. Proceedings of the Third Annual Meeting of the American Association of Pharmaceutical Scientists, Pharm. Res. 1988, 5(10), S-166.

Coleman, M.D., Fleckenstein, L., Geary, R.S., Brewer, T.G., Timony, G.A. and Mangold, D.J., (1988). The disposition of ethiofos in the isolated perfused rat liver. Proceedings of the American Society of Pharmacology Experimental Therapeutics Meeting, Montreal, Canada, October 1988.

Geary, R.S. and Stavchansky, S. (1987) In situ rat gut absorption of almitrine bismesylate in male sprague-dawley rats. Presented at the International Pharmaceutics Meeting, Netherlands, September 1987.

Stavchansky, S., Doluisio, J.T., Geary, R.S., Szalkowski, M.B., Bachand, R., and Johanson, W.G., (1986). Multiple oral administration of almitrine bismesylate to chronic obstructive pulmonary (COPD) patients. Presented at the 133rd Annual Meeting of the American Pharmacists Association, San Francisco, CA, February 1986.

Stavchansky, S., Doluisio, J.T., Geary, R.S., Szalkowski, M.B., Bachand, R. and Macleod, C.M., (1986). Multiple oral administration of almitrine bismesylate tablets to humans. Presented at the 133rd Annual Meeting of the American Pharmacists Association, San Francisco, CA, February 1986.

Stavchansky, S., Doluisio, J.T., Geary, R.S., Szalkowski, M.B., Bachand, R., and Macleod, C.M., (1986). Single oral administration of almitrine bismesylate to humans. Dose progression studies. Presented at the 133rd Annual Meeting of the American Pharmacists Association, San Francisco, CA, February 1986.

Stavchansky, S., Doluisio, J.T., Geary, R.S., Szalkowski, M.B., Bachand, R., and Macleod, C.M., (1986). Bioavailability of almitrine bismesylate film-coated tablets in man. Presented at the 133rd Annual Meeting of the American Pharmacists Association, San Francisco, CA, February 1986.

Geary, R.S., (1985). Comparison of locomotor activity induced by acute and chronic administration of phenylpropanolamine, caffeine, and d-amphetamine. Presented at the 132nd Annual Meeting of the American Pharmacists Association and the 38th National Meeting of the APS, San Antonio, TX, February 1985.

Geary, R.S., (1983). Acute and chronic effect of phencyclidine, phenylpropanolamine, caffeine, and d-amphetamine on locomotor activity. Presented at the 130th Annual Meeting of the American Pharmacists Association, Miami, FL, November 1983.

Geary, R.S., (1983). Comparisons of the locomotor activity produced by phencyclidine and d-amphetamine in CD-1 mice. Presented at the 116th Annual Meeting of the Texas Medical Association, Houston, TX, May 1983.

#### **PATENTS:**

Geary Richard S; Yu Zhengrong; Wedel Mark K; Tribble Diane (2008). Administering antisense oligonucleotides complementary to human apolipoprotein B. WO2008118883.

Geary Richard S; Tillman Llyoy G; Teng Ching-Leou; Weinback Susan P; Hardee Gregory E (2008). Bioadhesive compositions and methods for enhanced mucosal drug absorption. AU2002329825.

Tillman Lloyd G; Geary Richard S; Weinback Susan P; Hardee Gregory E (2008). Pulsatile release compositions and methods for enhanced gastrointestinal drug absorption. AU2002332647.

Bhanot Sanjay; Geary Richard S; McKay Robert; Monia Brett P; Seth Punit P; Siwkowski Andrew M; Swayze Eric E; Wanciewicz Edward (2008). Compounds and methods for modulating gene expression. US2008015162.

Siwkowski Andrew M; Wanciewicz Edward; Leedom Thomas A; Watts Lynnetta; Guha Mausumee; Monia Brett P; Griffey Richard H; Geary Richard S; Henry Scott; Levin Arthur (2007). Backbone modifications to modulate oligonucleotide targeting in vivo. US2007299028.

Bhanot Sanjay; Geary Richard S; McKay Robert; Monia Brett P; Seth Punit P; Siwkowski Andrew M; Swayze Eric E; Wancewicz Edward (2007). Compounds and methods for modulating expression ApoB. WO2007131238

Monia Brett P; Swayze Eric E; McKay Robert; Geary Richard S; Bhanot Sanjay; Siwkowski Andrew M; Wancewicz Edward; Seth Punit P (2007). Compounds and methods for modulating gene expression. AU2007258117

Bhanot Sanjay; Monia Brett P; Geary Richard S; Kjems Lise Lunt (2007). Antisense modulation of PTP1B expression. EP1807093.

Geary Richard S; Yu Zhengrong; Crooke Rosanne M (2007). Antisense modulation of apolipoprotein B expression. EP1786472.

Bhanot Sanjay; Monia Brett P; Geary Richard S; Kjems Lise L (2006). Antisense modulation of PTP1B expression. US2006089325.

Hardee, G.E., Geary, R.S., Levin, A.A., Templin, M.V., Howard, R., Mehta, R.C. (2000) Liposomal Oligonucleotide Compositions for Modulating ras Gene Expression. US6083923.

Geary, R.S. and Schlameus, H.W. (1996). Microparticulate pharmaceutical delivery system. US5505967.

Geary, R.S. and Schlameus, H.W. (1995). Microparticulate pharmaceutical delivery system for delivery to Peyer's glands. US5382435.

Geary, R. (1992). Enhancement of absorption of radioprotective ethiofos drugs using chelating agents. US5167947.

### **PROFESSIONAL MEMBERSHIPS:**

- 1) Society of Toxicology (SOT)
- 2) American Association of Pharmaceutical Scientists (AAPS)
- 3) American Society for Clinical Pharmacology & Therapeutics (ASCPT)
- 4) Rho Chi Honor Society